Asploro Journal of Biomedical and Clinical Case Reports
(ISSN: 2582-0370)
Mini Review
DOI: https://doi.org/10.36502/2021/ASJBCCR.6237

Trend for Clinical Use of Metabolic Associated Fatty Liver Disease (MAFLD)

Hiroshi Bando[1,2*]
[1]*Medical Research/Tokushima University, Tokushima, Japan*
[2]*Japan Masters Athletics, Tokushima Division, Board, Tokushima, Japan*

Corresponding Author: **Hiroshi BANDO, MD, PhD, FACP** ORCID iD
Address: Tokushima University /Medical Research, Nakashowa 1-61, Tokushima 770-0943, Japan. Email: pianomed@bronze.ocn.ne.jp
Received date: 24 February 2021; **Accepted date**: 21 April 2021; **Published date**: 30 April 2021

Citation: Bando H. Trend for Clinical Use of Metabolic Associated Fatty Liver Disease (MAFLD). Asp Biomed Clin Case Rep. 2021 Apr 30;4(2):99-102.

Abstract

The problems among obesity, diabetes mellitus (DM), fatty liver, metabolic dysfunction have been prevalent, and diagnostic criteria as non-alcoholic fatty liver disease (NAFLD) has been used in practice. When diagnosing NAFLD, to exclude other related liver diseases was necessary, including excessive alcohol intake. The international experts proposed the proper term from NAFLD to metabolic associated fatty liver disease (MAFLD). MAFLD criteria include the evidence of the presence of hepatic steatosis associated with three situations. They are obesity/overweight, presence of Type 2 DM (T2DM), or metabolic impaired function, which were studied in the light of pathophysiology, epidemiology, diagnosis and pharmacotherapy.

Keywords

Fatty Liver, Non-Alcoholic Fatty Liver Disease, Metabolic Associated Fatty Liver Disease, Non-Alcoholic Steatohepatitis

Abbreviations

NAFLD: Non-Alcoholic Fatty Liver Disease; MAFLD: Metabolic Associated Fatty Liver Disease; NASH: Non-Alcoholic Steatohepatitis

As the prevalence of obesity and type 2 diabetes mellitus (T2DM) has been increasing worldwide, fatty liver disease from metabolic dysfunction has been a global medical and health problem [1]. Especially, it was observed in early stages preceding the T2DM development. The problems among fatty liver, T2DM, metabolic syndrome have been important. Further, diagnostic criteria of non-alcoholic fatty liver disease (NAFLD) was common for usual practice of medicine [2].

NAFLD has affected approximately one quarter of adult population across the world, and brought medical, health and economic burden to many societies [2,3]. The effective pharmacotherapy for NAFLD has not been approved until now [4]. Higher NAFLD prevalence would be from several elements, such as excess carbohydrate intake, elevated calorie energy intake, decreased physical activity, habit of sedentary behavior, imbalance of diet and exercise, and so on [5]. Along with this tendency, health situation of adult has

been not satisfactory, even if the adult shows normal BMI in the affluent country [6,7].

NAFLD has recently shown higher ratio of the cause for chronic liver disease [2]. Regarding NAFLD in most guidelines, it is defined for the evidence of steatosis in 5%< of existing hepatocytes by medical imaging and/or histological examination [8]. Furthermore, it is important to show the situation of the absence in several causes including alcohol, B or C type of viral hepatitis, some kinds of hereditary liver diseases, or steatogenic medication for long term [9].

This diagnostic way has been adopted as an exclusive method, and for which liver biopsy would be the golden standard. It covers a spectrum for progressive liver diseases including steatosis to fibrosis, cirrhosis, nonalcoholic steatohepatitis (NASH) and hepatocellular carcinoma (HCC) [10]. It was well-known that it is clearly associated with metabolic dysfunction, where several components co-exist for abdominal obesity, hypertension, dyslipidemia and hyperglycemia [11]. As the existing ratio of NAFLD grows dramatically, there are urgent clinical problems [12]. They include i) the absence of clear nomenclature of the fatty liver due to non-alcohol use, ii) the lack of positive diagnosis with proper definition, iii) no approved medical agents for this disease, etc.

From statistic point of view, NAFLD has been found about 25% of the population worldwide [2,3]. According to the previous data, diabetics have chronic liver disease associated with about three-fold higher risk, which is mainly from non-alcohol or non-virus etiology leading to NAFLD [13]. NAFLD prevalence in T2DM shows up to 55.5%, which is more than twice than general people [14]. A recent meta-analysis data showed the prevalence of NAFLD as follows: general people 29.8%, T2DM 51.8%, non-diabetic 30.7%, obesity 66.2% and lean 11.7% [15]. As obesity shows rising trend from 2%-7% in 2000-2014, NAFLD showed increase in parallel [16]. Further, obesity and T2DM showed the elevated risk of progression for NASH, cirrhosis and HCC [17,18]. Consequently, growing epidemic situation of obesity and T2DM will bring increasing prevalence for NAFLD across the world [19].

Related to NAFLD, a panel of international experts was gathered from 22 countries [3]. The experts have proposed a changing medical term from NAFLD to new medical term, which is metabolic associated fatty liver disease (MAFLD). They reached a consensus that the term NAFLD would not reflect proper knowledge and that MAFLD would be more appropriate from terminological point of view. The new definition of MAFLD puts emphasis on the important function from metabolic aspect. In comparison with former NAFLD, newly summarized definition of MAFLD is supposed to include wider perspective. MAFLD criteria showed the evidence of hepatic steatosis found with the following three situations. They are obesity/overweight, T2DM presence, and/or the evidence of metabolic dysfunction (dysregulation) [20]. There are some differences of shared features between the words of NAFLD and MAFLD, in the light of pathophysiology, epidemiology, diagnosis and pharmacotherapy.

Similar to previous medical term NAFLD, MAFLD has represents hepatic manifestation for multisystem disorder. It shows heterogeneous factors in underlying cause, symptom and signs, clinical outcomes and progress course [13]. However, due to the complex pathophysiological aspects, a single diagnostic test is not likely to be available. Metabolic syndrome contains some definitions, and it seems necessary to develop the new criteria for diagnosing MAFLD in this way [21,22].

When diagnosing MAFLD, to exclude the other chronic liver diseases is necessary, including excessive alcohol intake [23]. With the elucidation of the pathophysiological processes causing to MAFLD, it would be increasingly understood that the existence of generalized metabolic syndrome seems to exist at the fundamental level. As a result, MAFLD is recognized for an independent disease that guarantees a positive diagnostic process, rather than excluding other diseases. Furthermore, the prevalence of MAFLD has been elevated, which makes it possible to exist in combination of other chronic liver diseases. Therefore, the method of excluding comorbidities becomes inappropriate. From the above, MAFLD definition will be made not according to the exclusion criteria but from the set of additional positive criteria [3].

Regarding the proposal from the experts, the disease assessment and stratification of MAFLD severity should cover the wider area, which are beyond a simple dichotomous classification of non-steatohepatitis and steatohepatitis [20]. There are other proposals including a set of criteria for the definition of MAFLD associated liver cirrhosis, and a conceptual perspective for other possible causes for fatty live. Consequently, the distinction would be clarified for the distinction of diagnostic criteria and also the inclusion criteria for research and clinical trials. To reaching a certain consensus on MAFLD criteria will contribute the unification of the medical terms including the International Classification of Diseases (ICD)-coding, Disease-Related Groups (DRG), verification of clinical trials, development of liver research and the improvement of clinical care [20].

In summary, current topics concerning the changing term from NAFLD to MAFLD were described in this article. Some clinical trials are found concerning the inclusion criteria and endpoints [24]. Such studies will bring various initiatives evolving for clinical application of new nomenclature MAFLD definition.

Conflict of Interest

The author has read and approved the final version of the manuscript. The author has no conflicts of interest to declare.

References

[1] Shiha G, Alswat K, Al Khatry M, Sharara AI, Örmeci N, Waked I, Benazzouz M, Al-Ali F, Hamed AE, Hamoudi W, Attia D, Derbala M, Sharaf-Eldin M, Al-Busafi SA, Zaky S, Bamakhrama K, Ibrahim N, Ajlouni Y, Sabbah M, Salama M, Anushiravani A, Afredj N, Barakat S, Hashim A, Fouad Y, Soliman R. Nomenclature and definition of metabolic-associated fatty liver disease: a consensus from the Middle East and north Africa. Lancet Gastroenterol Hepatol. 2021 Jan;6(1):57-64. [**PMID**: 33181119]

[2] Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, George J, Bugianesi E. Global burden of NAFLD and NASH: trends, predictions, risk factors and prevention. Nat Rev Gastroenterol Hepatol. 2018 Jan;15(1):11-20. [**PMID**: 28930295]

[3] Eslam M, Sanyal AJ, George J; International Consensus Panel. MAFLD: A Consensus-Driven Proposed Nomenclature for Metabolic Associated Fatty Liver Disease. Gastroenterology. 2020 May;158(7):1999-2014.e1. [**PMID**: 32044314]

[4] Sarin SK, Kumar M, Eslam M, George J, Al Mahtab M, Akbar SMF, Jia J, Tian Q, Aggarwal R, Muljono DH, Omata M, Ooka Y, Han KH, Lee HW, Jafri W, Butt AS, Chong CH, Lim SG, Pwu RF, Chen DS. Liver diseases in the Asia-Pacific region: a Lancet Gastroenterology & Hepatology Commission. Lancet Gastroenterol Hepatol. 2020 Feb;5(2):167-28. Erratum in: Lancet Gastroenterol Hepatol. 2020 Mar;5(3):e2. [**PMID**: 31852635]

[5] Inoue Y, Qin B, Poti J, Sokol R, Gordon-Larsen P. Epidemiology of Obesity in Adults: Latest Trends. Curr Obes Rep. 2018 Dec;7(4):276-88. [**PMID**: 30155850]

[6] Stefan N, Schick F, Häring HU. Causes, Characteristics, and Consequences of Metabolically Unhealthy Normal Weight in Humans. Cell Metab. 2017 Aug 1;26(2):292-300. [**PMID**: 28768170]

[7] Araújo J, Cai J, Stevens J. Prevalence of Optimal Metabolic Health in American Adults: National Health and Nutrition Examination Survey 2009-2016. Metab Syndr Relat Disord. 2019 Feb;17(1):46-52. [**PMID**: 30484738]

[8] Wong VW, Chan WK, Chitturi S, Chawla Y, Dan YY, Duseja A, Fan J, Goh KL, Hamaguchi M, Hashimoto E, Kim SU, Lesmana LA, Lin YC, Liu CJ, Ni YH, Sollano J, Wong SK, Wong GL, Chan HL, Farrell G. Asia-Pacific Working Party on Non-alcoholic Fatty Liver Disease guidelines 2017-Part 1: Definition, risk factors and assessment. J Gastroenterol Hepatol. 2018 Jan;33(1):70-85. [**PMID**: 28670712]

[9] Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, Harrison SA, Brunt EM, Sanyal AJ. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018 Jan;67(1):328-57. [**PMID**: 28714183]

[10] Yki-Järvinen H. Non-alcoholic fatty liver disease as a cause and a consequence of metabolic syndrome. Lancet Diabetes Endocrinol. 2014 Nov;2(11):901-10. [**PMID**: 24731669]

[11] Huang TD, Behary J, Zekry A. Non-alcoholic fatty liver disease: a review of epidemiology, risk factors, diagnosis and management. Intern Med J. 2020 Sep;50(9):1038-47. [**PMID**: 31760676]

[12] Younossi Z, Tacke F, Arrese M, Chander Sharma B, Mostafa I, Bugianesi E, Wai-Sun Wong V, Yilmaz Y, George J, Fan J, Vos MB. Global Perspectives on Nonalcoholic Fatty Liver Disease and Nonalcoholic Steatohepatitis. Hepatology. 2019 Jun;69(6):2672-82. [**PMID**: 30179269]

[13] Byrne CD, Targher G. NAFLD: a multisystem disease. J Hepatol. 2015 Apr;62(1 Suppl):S47-64. [**PMID**: 25920090]

[14] Younossi ZM, Golabi P, de Avila L, Paik JM, Srishord M, Fukui N, Qiu Y, Burns L, Afendy A, Nader F. The global epidemiology of NAFLD and NASH in patients with type 2 diabetes: A systematic review and meta-analysis. J Hepatol. 2019 Oct;71(4):793-801. [**PMID**: 31279902]

[15] Wu Y, Zheng Q, Zou B, Yeo YH, Li X, Li J, Xie X, Feng Y, Stave CD, Zhu Q, Cheung R, Nguyen MH. The epidemiology of NAFLD in Mainland China with analysis by adjusted gross regional domestic product: a meta-analysis. Hepatol Int. 2020 Mar;14(2):259-69. [**PMID**: 32130675]

[16] Zhou J, Zhou F, Wang W, Zhang XJ, Ji YX, Zhang P, She ZG, Zhu L, Cai J, Li H. Epidemiological Features of NAFLD From 1999 to 2018 in China. Hepatology. 2020 May;71(5):1851-64. [**PMID**: 32012320]

[17] Rhee EJ. Nonalcoholic Fatty Liver Disease and Diabetes: An Epidemiological Perspective. Endocrinol Metab (Seoul). 2019 Sep;34(3):226-33. [**PMID**: 31565874]

[18] Polyzos SA, Kountouras J, Mantzoros CS. Obesity and nonalcoholic fatty liver disease: From pathophysiology to therapeutics. Metabolism. 2019 Mar;92:82-97. [**PMID**: 30502373]

[19] Li J, Zou B, Yeo YH, Feng Y, Xie X, Lee DH, Fujii H, Wu Y, Kam LY, Ji F, Li X, Chien N, Wei M, Ogawa E, Zhao C, Wu X, Stave CD, Henry L, Barnett S, Takahashi H, Furusyo N, Eguchi Y, Hsu YC, Lee TY, Ren W, Qin C, Jun DW, Toyoda H, Wong VW, Cheung R, Zhu Q, Nguyen MH. Prevalence, incidence, and outcome of non-alcoholic fatty liver disease in Asia, 1999-2019: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol. 2019 May;4(5):389-98. [**PMID**: 30902670]

[20] Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, Zelber-Sagi S, Wai-Sun Wong V, Dufour JF, Schattenberg JM, Kawaguchi T, Arrese M, Valenti L, Shiha G, Tiribelli C, Yki-Järvinen H, Fan JG, Grønbæk H, Yilmaz Y, Cortez-Pinto H, Oliveira CP, Bedossa P, Adams LA, Zheng MH, Fouad Y, Chan WK, Mendez-Sanchez N, Ahn SH, Castera L, Bugianesi E, Ratziu V, George J. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. J Hepatol. 2020 Jul;73(1):202-209. [**PMID**: 32278004]

[21] Whelton PK, Carey RM, Aronow WS, Casey DE Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ, Muntner P, Ovbiagele B, Smith SC Jr, Spencer CC, Stafford RS, Taler SJ, Thomas RJ, Williams KA Sr, Williamson JD, Wright JT Jr. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2018 Jun;71(6):1269-24. Erratum in: Hypertension. 2018 Sep;72(3):e33. [**PMID**: 29133354]

[22] American Diabetes Association. 2. Classification and Diagnosis of Diabetes: *Standards of Medical Care in Diabetes-2018*. Diabetes Care. 2018 Jan;41(Suppl 1):S13-27. [**PMID**: 29222373]

[23] Eslam M, Sanyal AJ, George J. Toward More Accurate Nomenclature for Fatty Liver Diseases. Gastroenterology. 2019 Sep;157(3):590-93. [**PMID**: 31158374]

[24] Siddiqui MS, Harrison SA, Abdelmalek MF, Anstee QM, Bedossa P, Castera L, Dimick-Santos L, Friedman SL, Greene K, Kleiner DE, Megnien S, Neuschwander-Tetri BA, Ratziu V, Schabel E, Miller V, Sanyal AJ; Liver Forum Case Definitions Working Group. Case definitions for inclusion and analysis of endpoints in clinical trials for nonalcoholic steatohepatitis through the lens of regulatory science. Hepatology. 2018 May;67(5):2001-12. [**PMID**: 29059456]

Keywords: Fatty Liver, Non-Alcoholic Fatty Liver Disease, Metabolic Associated Fatty Liver Disease, Non-Alcoholic Steatohepatitis